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The association between ambient temperature and the risk of preterm birth in China

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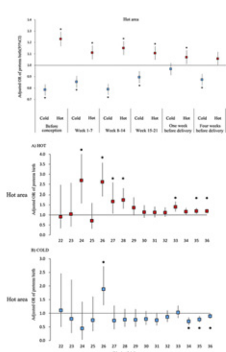
HIGHLIGHTS

- The largest study to date on the relationship between temperature and preterm birth in China.
- Covering a wide range of 132 cities in China.
- Long-term and short-term exposures to temperature at different stages of pregnancy were studied.
- Hot exposure may be a risk factor for preterm birth, and cold exposure may be a protective factor for preterm birth.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: With the gradual increase of global warming, the impact of extreme temperatures on health has become a focus of attention, however, its relationship with preterm birth remains unclear.
Objectives: To investigate the association between exposure to extreme temperatures and preterm birth.
Methods: Temperature exposures and birth outcomes of 1,020,471 pregnant women from 132 cities in China were investigated. The pregnancy process was divided into different pregnancy periods. Study areas were divided into three categories (cold, medium, and hot areas) according to the local average temperature by cluster analysis. Average temperature data for each province used in the cluster analysis came from the China Statistical Yearbook 2013. Logistic regression was used to compare the effects of exposure to hot and cold conditions on the outcomes of pregnancy in different periods and regions.
Results: A total of 1,020,471 singleton births were included, of which 73,240(7.2%) were preterm births. Compared with moderate temperatures (5th to 95th percentile), heat exposure (>95th percentile) in different periods of pregnancy increased the risk of preterm birth in hot areas. The most obvious increase was during the 3 months before pregnancy (odds ratio (OR) = 1.229, 95% confidence interval (CI): 1.166–1.295). In contrast to heat exposure, cold exposure (<5th percentile) in hot areas reduced the risk of preterm birth; the protective effect was most pronounced in the 3 months before pregnancy (OR = 0.784, 95% CI: 0.734–0.832). In medium and cold areas cold exposure also reduced the risk of preterm birth. The effect of exposure to extreme ambient temperatures throughout the entire pregnancy on preterm birth was similar to those of the periods above.
Conclusions: Acute and chronic exposure to extreme temperatures may affect the risk of preterm birth. Extreme heat is a risk factor for preterm birth and extreme cold is a protective factor.

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1. Introduction

Recent studies have shown that the incidence of preterm birth worldwide is about 10% (Beck et al., 2010), which is considered a major global health problem. The World Health Organization has defined preterm birth as a live baby who is born before 37 weeks of pregnancy (Listed, 1977). Preterm birth is an important cause of perinatal morbidity and mortality and may lead to a variety of complications, such as neurologic and developmental disabilities (Frey and Klebanoff, 2016). Many surviving preterm children also face life-long difficulties, including learning disabilities and vision and hearing problems (Marlow et al., 2005). Therefore, prevention of preterm birth is a serious and urgent challenge. Although many risk factors and interventions have been explored, preterm birth rates continue to increase in nearly all countries with reliable data (Blencowe et al., 2012); therefore, further study of the risk factors for preterm birth is required.

The increases in global warming and extreme weather have received much attention in recent years, and many studies have been conducted on diseases that may be related to environmental factors (Barnett, 2007). As a special population, the ability of pregnant women to maintain a balanced body temperature is very limited. Owing to the physical and mental stress caused by pregnancy, these women are more vulnerable to environmental factors (Flouris, 2011). The impact of extreme ambient temperature exposure during pregnancy is of great public health concern, and its potential relationship with preterm birth is particularly important.

The current findings regarding the relationship between ambient temperature and preterm birth are inconsistent. Research has shown that short-term heat exposure increases the risk of preterm birth (Patrizia et al., 2013). Extreme cold exposure had been found to raise the risk of preterm birth (He et al., 2016). Other studies have yielded the opposite conclusion that exposure to extreme cold temperatures is not associated with premature birth (Vicedo-Cabrera et al., 2015). These differing results may be related to differences in study design, geographic location, population, length of exposure window, cutoff value, and may also be related to regional adaptability, such as people from hot areas are more tolerant of heat than those from cold regions (Guo, 2014). The detailed mechanism of the influence of environmental temperatures on preterm birth remains to be elucidated; there is no clear conclusion at present.

There are a few studies on the relationship between long-term exposure to heat or cold and birth outcomes; however, there are no studies on the relationship between exposure to environmental factors and preterm birth in different periods of pregnancy for the entire Chinese population. The purpose of this study was to explore the effects of exposure to extreme environmental temperatures during pregnancy on preterm birth.

2. Methods

2.1. Study population

The data used in the study were obtained from the National Free Pre-pregnancy Checkups Project (NFPCP). The NFPCP is a national health service that has been supported by the National Health and Family Planning Commission and the Ministry of Finance of the People's Republic of China since 2010, aiming to provide free pre-pregnancy medical examinations and follow-up of pregnancy outcomes for couples of childbearing age throughout the country. The NFPCP covered only rural couples from 2010 to 2012 and was further expanded to urban couples in 2013. Our study covered 132 cities in 30 provinces of China; the details are given in Fig. 1.

Women aged 15 to 49 years old who participated in the NFPCP between January 2010 and December 2013 were included in this study. Participants were enrolled by trained staff. Date of Age, number of previous pregnancies, alcohol consumption, exposure to secondhand smoke, and other information were collected by qualified nurses using structured questionnaires in face-to-face interviews. Physical characteristics of women of childbearing age, such as pre-pregnancy body mass index, were collected through physical examinations, and pregnancy outcome information was obtained by follow-up investigation for all participants. A total of 1,122,456 women with pregnancy outcome data were enrolled in the NFPCP. The analysis was restricted to all singleton births. After removal of multiple pregnancies, miscarriages and stillbirths, a total 1,020,471 women were included in the current analysis. Of these 955,284(93.6%) were rural inhabitants and 65,187(6.4%) were urban inhabitants. The details are given in Fig. 2.

The Institutional Research Review Board of the National Research Institute for Family Planning approved the study protocols and forms, in accordance with the relevant guidelines and regulations. Informed consent was obtained from all NFPCP participants.

2.2. Temperature exposure

Hourly temperature and humidity data for each city were obtained from the National Meteorological Information Center of the China Meteorological Administration and were linked to each woman of childbearing age, based on residential address data collected by the NFPCP.

Because the etiology threshold window for the effects of temperature exposure on risk of preterm birth is still unclear, several exposure windows were explored. The windows of average daily temperature exposure were set to 3 months before pregnancy (91 days before the last menstrual date), the first 1–7 weeks of pregnancy, weeks 8–14 of pregnancy, weeks 15–21 of pregnancy, and the entire pregnancy period (length of the entire pregnancy is estimated from the menstrual date and date of delivery), to explore the effect of long-term ambient temperature exposures on preterm birth (Ha et al., 2016). In addition, to explore the effects of short-term exposure on preterm birth, the exposure windows were also set to 1 week before delivery and 4 weeks before delivery (Strand et al., 2012).

As the study covered a number of cities across China, temperature exposures were categorized by local temperature distributions among study participants in each pregnancy window, to reflect regional adaptability. An average temperature distribution for each location and each pregnancy window was created, and the exposures were defined based on the following cutoff values: cold (<5th percentile), hot (> 95th percentile), and moderate (5th to 95th percentile) (Liang et al., 2016). The study areas were divide into three categories as cold, medium, and hot areas according to the local average temperature by cluster analysis. Average temperature data for each province used for cluster analysis came from the China Statistical Yearbook 2013; details are provided in Table A1.

2.3. Outcome and covariates

All results and covariate information were obtained from the NFPCP. The primary outcome of this study was preterm birth, defined as delivery at <37 weeks, compared with full-term birth(delivery at ≥37 weeks) (van Vliet et al., 2017). The gestational age was calculated as the number of weeks between the date of the last menstrual period and date of delivery. Covariate variables included maternal age, body mass index before pregnancy, infant sex, exposure to alcohol and secondhand smoke during pregnancy, number of previous pregnancies, the month of pregnancy, humidity, and the average per capita gross domestic product (GDP) of each city from 2010 to 2013. Maternal age was categorized into several groups: <20, 20–24, 25–29, 30–34 and ≥35 years. Body mass index before pregnancy was calculated as weight in kilograms divided by height in meters squared (kg/m^2) and categorized as underweight (<18.5), normal weight (18.5–23.9), overweight (24–27.9) and obese (≥28) (Ramos et al., 2017).

Fig. 1. Spatial distribution of study sites, based on cluster analysis of the average temperature in each province, from the China Statistical Yearbook 2013.

2.4. Statistical analysis

Logistic regression was used to determine the odds ratios (ORs) and 95% confidence intervals (CIs) of preterm birth associated with extreme temperature exposures, using the full-term birth group as a comparison. This was achieved by comparing the heat and cold exposure groups defined by the cutoff values mentioned above to the moderate exposure group for different pregnancy windows, adjusting for covariates such as maternal age, body mass index before pregnancy, infant sex, exposure to alcohol and secondhand smoke during pregnancy, number of previous pregnancies, the month of pregnancy, humidity, and average per capita GDP of each city.

The temperature exposure of the entire pregnancy period was not directly compared because the pregnancy lengths of preterm births and full-term births are different. Instead, the entire pregnancy temperature exposure of preterm birth was compared to that of ongoing pregnancies limited to the same length of gestation at a given week (range: weeks 22–36). For instance, the average temperatures throughout the pregnancy of preterm birth deliveries at week 30 were compared to all ongoing pregnancies using temperature exposures up to week 30. The temperature distribution was based on the pregnant women at risk of delivery in each week, and the cutoff values used to define heat and cold were distinguished by region and week. The risk estimate can be interpreted as the risk of delivery in a given week associated with the entire pregnancy exposures up to that week (Ha et al., 2016).

3. Results

A total of 1,020,471 singleton births were included in the study; the gestational age ranged from 20 to 42 weeks. Of these, 73,240 (7.2%) were preterm births, and 947,231 (92.8%) were term births. The frequency of preterm births was higher among pregnant women aged 30–34 years and under 24 years than those of other ages and was higher in the following groups: male infant sex, exposure to secondhand smoke, and history of previous pregnancy. On the contrary, pregnant women with normal weight had a lower rate of preterm birth. Detailed characteristics of the study population are shown in Table 1.

Table 2 describes the number of women exposed to different ambient temperatures during different periods of pregnancy and the adjusted associations between ambient temperatures and preterm birth in different regions. In hot areas, heat exposure during the period 3 months before pregnancy was associated with a 22.9% (95% CI: 16.6%–29.5%) greater risk of preterm birth; the risk of early delivery was also higher in other periods of pregnancy, ranging from 6.9% to 15.0%. Compared with moderate temperatures, exposure to cold in weeks 8–14 and in the 3 months before pregnancy was associated with a 21.2% (95% CI: 16.2%–25.9%) and 21.6% (95% CI: 16.8%–26.8%) lower risk of preterm birth, respectively. Cold exposures in other periods of pregnancy also reduced the risk of preterm birth; only exposure in the week before delivery was not associated with early delivery. In medium areas, cold exposure in weeks 8–14 and weeks 15–21 was associated with a 14.4% (95% CI: 9.5%–19.0%) and 7.7% (95% CI: 2.5%–12.6%) lower risk

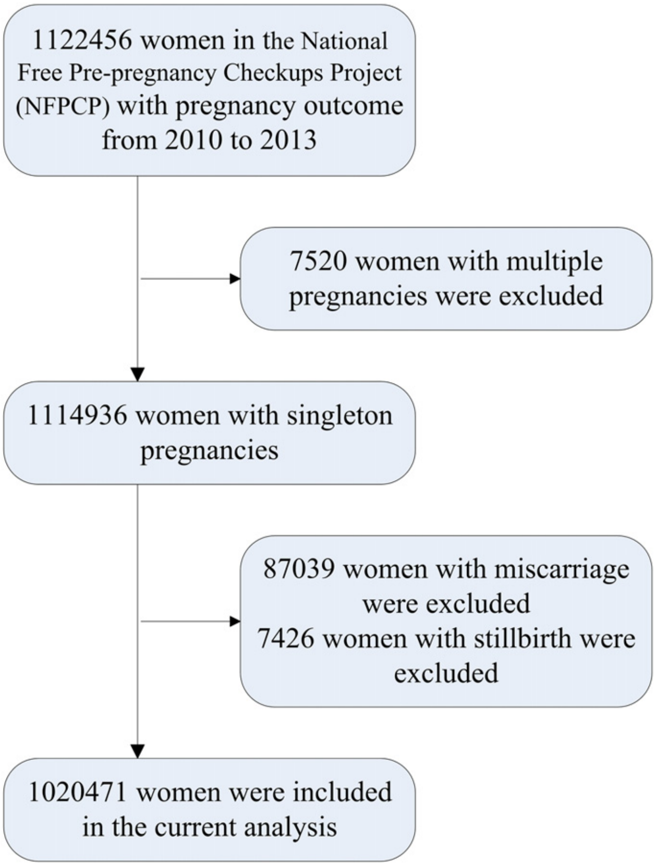

Fig. 2. Flow chart of study population.

Table 1
Characteristic of study population.

Characteristics	Total	Preterm birth (<37 weeks)		Term birth (≥37 weeks)		
	$N=$ 1,020,471	$N=$ 73,240(7.2%)		$N=$ 947,231(92.8%)		
	n	n	%	n	%	P
Maternal age						<0.001
<20	12,561	1074	8.6	11,487	91.4	
20–24	441,043	31,858	7.2	409,185	92.8	
25–29	406,121	28,620	7.0	377,501	93.0	
30–34	125,580	9181	7.3	116,399	92.7	
≥35	35,166	2507	7.1	32,659	92.9	
Pre-pregnancy BMI						<0.001
<18.5	146,982	10,740	7.3	136,242	92.7	
18.5–23.9	737,148	51,927	7.0	685,221	93.0	
24–27.9	113,398	8747	7.7	104,651	92.3	
≥28	22,943	1826	8.0	21,117	92.0	
Baby's sex						<0.001
Male	537,145	40,094	7.5	497,051	92.5	
Female	483,326	33,146	6.9	450,180	93.1	
Second-hand smoking						0.042
Yes	149,936	10,560	7.3	134,376	92.7	
No	875,535	62,680	7.2	812,855	92.8	
Alcohol use						0.033
Yes	31,150	2153	6.9	28,997	93.1	
No	989,321	71,087	7.2	918,234	92.8	
Number of previous pregnancies						<0.001
0	583,013	39,307	6.7	543,706	93.3	
1	315,922	24,961	7.9	290,961	92.1	
≥2	121,536	8972	7.4	112,564	92.8	
Month of conception						<0.001
January	94,907	6940	7.3	87,967	92.7	
February	86,437	6774	7.8	79,663	92.2	
March	83,673	6390	7.6	77,283	92.4	
April	79,812	5931	7.4	73,881	92.6	
May	84,491	6019	7.1	78,472	92.9	
June	77,964	5518	7.1	72,446	92.9	
July	82,167	5889	7.2	76,278	92.8	
August	85,210	6017	7.1	79,193	92.9	
September	86,890	5718	6.6	81,172	93.4	
October	88,865	5993	6.7	82,872	93.3	
November	83,346	5696	6.8	77,650	93.2	
December	86,709	6355	7.3	80,354	92.7	
Region						<0.001
Hot area	393,547	28,507	7.2	365,040	92.8	
Medium area	488,252	32,300	6.6	455,952	93.4	
Cold area	138,672	12,433	9.0	126,239	91.0	

Abbreviation: BMI, body mass index.

of preterm birth, respectively. Heat exposure during the 4 weeks before delivery increased the risk of preterm birth whereas exposure during the 3 months before pregnancy was a protection factor. In cold area, only cold exposures during weeks 15–21 and three months before pregnancy were protection factors of preterm birth. The cutoff values used to determine heat and cold exposures in different regions and different periods of pregnancy are shown in Table A2.

Fig. 3 shows the relationship between entire pregnancy temperature exposures and preterm birth. It should be noted that entire pregnancy temperature exposures of ongoing pregnancies were limited to a given week. In hot areas, long-term exposures to hot conditions throughout the pregnancy up to the week of delivery were associated with an increased risk of preterm birth at weeks 24, 26–28, 33, and weeks 35–36. Cold exposures were associated with a reduction in risk of preterm births at weeks 34–36 and an increased risk at week 26. In medium areas, the effect of heat and cold exposure on preterm birth was similar to that in hot areas, most effects in cold areas were not significant. The detailed data are presented in Table A3.

4. Discussion

In this study, exposure to cold temperatures in hot areas from the 3 months before pregnancy to 21 weeks of gestation had a protective effect on preterm birth; the protective effects were strongest in the period of 3 months before pregnancy. By contrast, exposure to hot environments in hot areas increased the risk of preterm birth; this increased risk was most pronounced in the 3 months before pregnancy. Acute exposure to cold in the 4 weeks before delivery reduced the risk of preterm birth, and acute exposure to heat in the week before delivery increased the risk of preterm birth. In medium areas, only heat exposure in the 4 weeks before delivery increased the risk of preterm birth; cold exposure at weeks 8–21 was a protective factor. Heat exposure in cold areas had no significant effect, and cold exposure was also a protective factor. Analysis of exposures to ambient temperatures throughout the whole pregnancy showed that prolonged exposure to cold conditions reduced the risk of preterm birth. Cold exposure for the first 34 weeks of pregnancy had the strongest protective effect on early delivery in hot areas; however, long-term exposure to hot environments increased the risk of preterm birth. These results indicated that exposure to extreme temperatures during pre-pregnancy and different periods of pregnancy had an impact on the occurrence of preterm birth, with cold being a protective factor and heat a risk factor. In addition, the variance of temperatures in hot areas is greater than in cold areas, which may also be why, compared with cold regions, extreme temperature exposure in hot areas is more strongly associated with preterm birth.

There have been many studies on the effects of short-term exposure to hot conditions before delivery on birth outcomes. A study in California showed that heat exposure within 3 days before delivery increased infant mortality (Basu et al., 2010). Other studies found that exposure to hot environments within the 4 weeks before delivery increased the risk of preterm birth (He et al., 2016; Strand et al., 2012). These results are in line with our findings in hot and medium areas, suggesting that

Table 2
Adjusted odds ratios[a] of preterm birth associated with extreme ambient temperatures, by pregnancy window.

Region	Pregnancy windows	Temperature	No. of preterm birth (%)	*OR*	*95%CI*	*P*
Cold area						
	Preconception	Moderate	11,268(9.0)	1.000		
		Cold	541(8.1)	0.894	0.814–0.982	0.020
		Hot	624(9.2)	0.934	0.934–1.107	0.702
	Weeks 1–7	Moderate	11,214(9.0)	1.000		
		Cold	590(8.7)	0.967	0.884–1.057	0.455
		Hot	629(9.3)	1.047	0.961–1.141	0.292
	Weeks 8–14	Moderate	11,218(9.0)	1.000		
		Cold	587(8.7)	0.930	0.850–1.018	0.116
		Hot	628(9.2)	1.043	0.958–1.135	0.335
	Weeks 15–21	Moderate	11,228(9.0)	1.000		
		Cold	572(8.5)	0.895	0.816–0.980	0.017
		Hot	633(9.4)	1.063	0.976–1.157	0.160
	four weeks before delivery	Moderate	11,250(9.0)	1.000		
		Cold	568(8.4)	0.933	0.853–1.021	0.133
		Hot	615(9.0)	1.022	0.936–1.116	0.633
	one week before delivery	Moderate	11,245(9.0)	1.000		
		Cold	575(8.4)	0.943	0.862–1.031	0.198
		Hot	613(9.1)	1.019	0.933–1.113	0.678
Medium area						
	Preconception	Moderate	29,266(6.6)	1.000		
		Cold	1549(6.5)	0.956	0.906–1.010	0.107
		Hot	1485(6.2)	0.943	0.894–0.995	0.034
	Weeks 1–7	Moderate	29,207(6.6)	1.000		
		Cold	1608(6.7)	1.005	0.953–1.060	0.845
		Hot	1485(6.2)	0.984	0.932–1.039	0.562
	Weeks 8–14	Moderate	29,294(6.6)	1.000		
		Cold	1515(6.3)	0.856	0.810–0.905	<0.001
		Hot	1491(6.3)	0.968	0.917–1.021	0.230
	Weeks 15–21	Moderate	29,169(6.6)	1.000		
		Cold	1575(6.6)	0.923	0.874–0.975	0.004
		Hot	1556(6.5)	0.979	0.929–1.032	0.433
	four weeks before delivery	Moderate	28,978(6.6)	1.000		
		Cold	1607(6.7)	0.996	0.944–1.050	0.871
		Hot	1715(7.2)	1.157	1.098–1.219	<0.001
	one week before delivery	Moderate	29,052(6.6)	1.000		
		Cold	1640(6.8)	1.026	0.973–1.081	0.343
		Hot	1608(6.7)	1.041	0.987–1.098	0.137
Hot area						
	Preconception	Moderate	25,665(7.2)	1.000		
		Cold	1187(6.2)	0.784	0.734–0.832	<0.001
		Hot	1655(8.6)	1.229	1.166–1.295	<0.001
	Weeks 1–7	Moderate	25,706(7.2)	1.000		
		Cold	1279(6.6)	0.853	0.803–0.906	<0.001
		Hot	1522(7.9)	1.110	1.052–1.172	<0.001
	Weeks 8–14	Moderate	25,743(7.3)	1.000		
		Cold	1191(6.2)	0.788	0.741–0.838	<0.001
		Hot	1573(8.1)	1.150	1.090–1.213	<0.001
	Weeks 15–21	Moderate	25,655(7.2)	1.000		
		Cold	1321(6.8)	0.895	0.844–0.949	<0.001
		Hot	1531(7.9)	1.106	1.048–1.167	<0.001
	four weeks before delivery	Moderate	25,775(7.3)	1.000		
		Cold	1286(6.6)	0.873	0.823–0.925	<0.001
		Hot	1446(7.4)	1.056	0.998–1.118	0.060
	one week before delivery	Moderate	25,652(7.2)	1.000		
		Cold	1395(7.2)	0.965	0.912–1.021	0.211
		Hot	1460(7.5)	1.069	1.010–1.132	0.022

Notes: The number of preterm births is presented as frequency (percent). Cold, moderate, and hot were defined as <5th, 5-95th, and >95th percentile of the distribution of temperature by site. The study areas were divided into three categories as cold, medium, and hot areas according to the local average temperature by cluster analysis. Abbreviations: OR, odds ratio; CI, confidence interval.

[a] The model was adjusted for all covariates in Table 1, humidity, region, and average per capita GDP.

attention should be given to the impact of short-term environmental temperature exposures before delivery. Little research has been done on the effects of long-term exposure to hot conditions on preterm birth. A cohort study in the United States showed that exposure to hot environments in the 3 months before pregnancy and throughout the entire pregnancy process increased the incidence of preterm birth (Ha et al., 2016), which was consistent with our findings. Our study also considered that heat exposure during the e months before pregnancy should be particularly concerning, because the sensitivity to temperature among pregnant women is high in this period. Moreover, since sperm motility has an impact on pregnancy outcomes (Shulman et al., 1998) and the production and maturation of sperm requires about 3 months, we speculate that exposure to extreme temperatures during the 3 months before pregnancy influences the quality of sperm and therefore affects the occurrence of preterm birth. These results all suggest that exposure to heat exposures increases the risk of preterm birth. In addition, the impact of heat exposure on preterm birth in hot areas may have a time trend, that is, the effect of temperature on

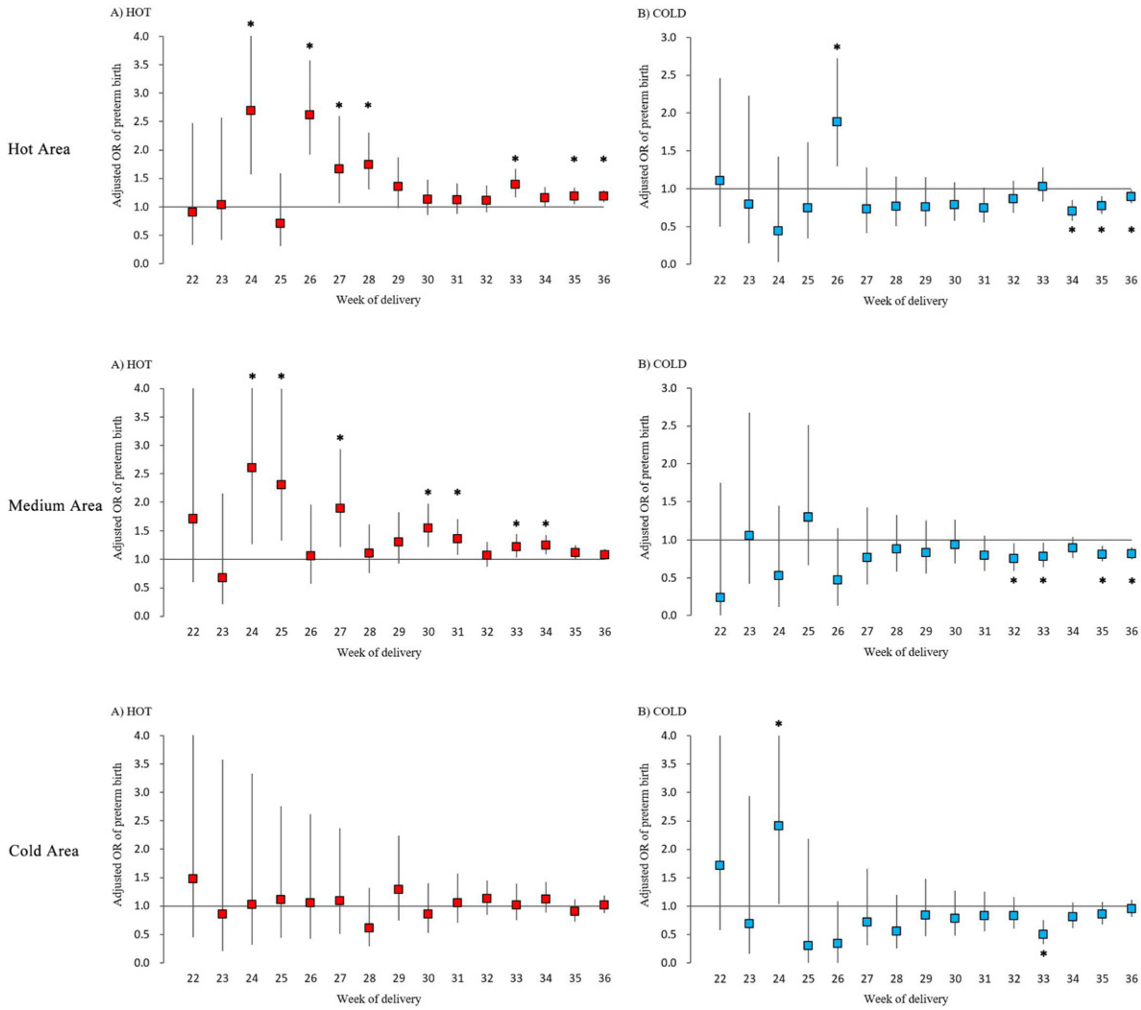

Fig. 3. Adjusted odds ratios of preterm birth associated with heat (A) and cold (B) exposures during the entire pregnancy, by week of delivery. Models adjusted for all covariates in Table 1, humidity, average per capita GDP, and study site. Asterisks indicate statistical significance at alpha <0.05.

preterm birth is gradually reduced with the progression of pregnancy, which may be related to the phenomenon that women with longer pregnancies may better protect themselves from exposure to extreme temperatures. Contrary to the abovementioned results, a time series analysis in Shenzhen, China concluded that heat exposure was a protective factor for preterm birth (Liang et al., 2016). Previous studies have suggested that this may be related to the hotter geographical location of Shenzhen and that the local population was more resistant to hot environments; there is a possibility that pregnant women living in hot areas are more likely to stay indoors in hot weather. However, our study found the same tendency during the 3 months before pregnancy in medium areas, where extreme ambient temperatures were lower than those of Shenzhen. The reasons for this situation require further study.

There have been several studies on the effects of exposure to cold conditions on preterm birth, but the results have been in consistent. Cohort studies in the United States (Ha et al., 2016) and in Shenzhen (Liang et al., 2016), and Guangzhou (He et al., 2016) in China showed that short-term exposure to cold conditions before delivery increased the risk of preterm birth On the other hand cohort studies in Rome (Patrizia et al., 2013) and Sweden (Vicedo-Cabrera et al., 2015) suggested that short-term cold exposure had no effect on preterm delivery. Compared with pregnant women exposed to moderate temperatures, some research has reported that there is no increase or decrease in the risk of preterm birth among those who are exposed to cold temperatures throughout their pregnancy (Ha et al., 2016). In contrast to these results, we concluded that cold exposure, both before and during pregnancy, had a protective role in the occurrence of preterm birth in all study areas especially in hot areas. The reason for this may be the low temperatures in hot areas were similar to the medium temperatures in other areas, which can be considered relatively suitable temperatures. However, Fig. 3 shows that exposure to cold conditions throughout the pregnancy up to 26 weeks' gestation increased the risk of preterm births in hot areas. This result may be related to the fact that >80% of women who delivered at this gestational age were from Hunan and Jiangxi provinces, which are located to the north in relatively hot areas and have comparatively lower cold temperatures, which are more likely to be a risk factor. These very different results suggested that the effects of cold exposure among pregnant women requires further in-depth investigation and pre-pregnancy cold exposure should be a priority.

The mechanism of the effect of exposure to extreme temperatures on preterm birth has been unclear. Some studies have suggested that acute hot stress can reduce uterine blood flow and increase serum oxytocin, thereby changing the metabolic pathway of the fetus from synthetic metabolism into a catabolic state and causing preterm birth or other adverse outcomes (Dreiling et al., 1991). The decline in blood flow may also lead to decreased maternal oxygen carrying capacity, uterine oxygen shortage, and blood viscosity (Chambers et al., 1998). Changes in uterine blood flow and vaginal flora may increase the risk of maternal infection, leading to early uterine contraction, premature rupture of membranes, and may finally cause early delivery (Zou et

al., 2011). There have also been studies showing that it may take a month from the start of changes in the vaginal flora until inflammation occurs, in line with the time span of extreme ambient temperature exposure during the 4 weeks before delivery to the occurrence of premature birth, which may be the potential cause of the different results between exposures during 4 weeks and week before pregnancy (Cheng et al., 2016). Furthermore, studies have shown that since the fetus is more sensitive to high temperature environments, heat exposure during pregnancy may adversely affect pregnancy outcomes, such as by increasing the risk of fetal hypospadias (Hwang et al., 2011; Kilinc et al., 2016). These findings suggest that pregnant women who are exposed to hot environments require more attention and measures must be taken to reduce heat exposure. The mechanism of cold exposure effects on pregnancy outcome has not yet been determined, and is a topic for further exploration.

Global warming has been gaining more and more attention with the rise in global average temperatures, now considered a potential global disaster (Nauels, 2014). Studies have shown that China's climate has been greatly affected by the process of global warming, and high temperatures in China will continue to have an increasing trend in the future (Solomon et al., 2007). Because pregnant women are more susceptible to high temperatures, elevated ambient temperatures may have a significant impact on pregnancy and delivery (Basu et al., 2010). As a developing country, the development of public health in China must be improved, to more closely approximate that of developed countries. Reducing preterm birth is a major public health challenge for China at present, and the relevant scientific research and policy investment must be strengthened as soon as possible.

This study had some limitations. Information on gestational complications was not collected, which may be a potential influencing factor. In addition, participants' income was not investigated; income may be an important factor affecting pregnancy outcome because it determines the level of care available to pregnant women; however, we included average per capita GDP to reflect the living standard of pregnant women in the study areas. Mean temperatures in different periods of pregnancy were used for the analysis; the impact of maximum and minimum temperatures on pregnant women was not investigated, which remains to be examined. Air pollution is an important factor in China, and many studies have reported that air pollutions is related to preterm birth. One study showed that air pollution interacts with temperature, and the effect of air pollution on health is most pronounced at extreme temperatures (Roberts, 2004). We speculated that the risk of preterm birth may increase with increased exposure to air pollution. Because we did not collect extensive national air pollution data from 2010 to 2013, we aim to consider air pollution measures in future studies. Furthermore, in this study, the proportion of rural inhabitants was 93.6%, higher than the proportion of China's total rural population, 70.9%. This is related to the fact that the NFPCP was available only for rural populations between 2010 and 2012; however, the NFPCP began to cover urban populations in 2013, and future follow-up studies will include more urban population data. This study also had some important strengths. First, the study population was large enough to be representative of the population of China, and to date, there has not been such an extensive and large-scale cohort study of preterm birth. In addition, the residential information collected can be used to effectively estimate the scope of participant activities, to obtain the ambient temperature exposure of each participant. Lastly, humidity, age, pregnancy month, average per capita GDP, and regions were adjusted for as potential risk factors.

5. Conclusion

In this study in China, exposures to high temperatures increased the risk of preterm birth, and low temperature exposure was a protective factor for early delivery. In view of the current global warming trend, research of preterm birth should be given priority, to help in establishing more effective policies.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.scitotenv.2017.09.104.

References

Barnett, A.G., 2007. Temperature and cardiovascular deaths in the us elderly: changes over time. Epidemiology 18 (3), 369–372.
Basu, R., Malig, B., Ostro, B., 2010. High ambient temperature and the risk of preterm delivery. Am. J. Epidemiol. 172 (10), 1108.
Beck, S., Wojdyla, D., Say, L., Betran, A.P., Merialdi, M., Requejo, J.H., et al., 2010. The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. Bull. World Health Organ. 88 (1), 31.
Blencowe, H., Cousens, S., Oestergaard, M., Chou, D., Moller, A.B., Narwal, R., et al., 2012. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet 379 (9832), 2162–2172.
Chambers, C.D., Johnson, K.A., Dick, L.M., Felix, R.J., Jones, K.L., 1998. Maternal fever and birth outcome: a prospective study. Birth Defects Res. A Clin. Mol. Teratol. 58 (6), 251.
Cheng, Y.P., Feng, Y.L., Duan, X.L., Zhao, N., Wang, J., Li, C.X., et al., 2016. Ambient pm2.5 during pregnancy and risk on preterm birth. Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi 37 (4), 572.
Dreiling, C.E., Rd, C.F., Brown, D.E., 1991. Maternal endocrine and fetal metabolic responses to heat stress. J. Dairy Sci. 74 (1), 312–327.
Flouris, A.D., 2011. Functional architecture of behavioural thermoregulation. Eur. J. Appl. Physiol. 111 (1), 1–8.
Frey, H.A., Klebanoff, M.A., 2016. The epidemiology, etiology, and costs of preterm birth. Semin. Fetal Neonatal Med. 21 (2), 68–73.
Guo, Y., 2014. Global variation in the effects of ambient temperature on mortality: a systematic evaluation. Epidemiology 2014 (5), 1–9.
Ha, S., Liu, D., Zhu, Y., Kim, S.S., Sherman, S., Mendola, P., 2016. Ambient temperature and early delivery of singleton pregnancies. Environ. Health Perspect. 125 (3), 453–459.
He, J.R., Liu, Y., Xia, X.Y., Ma, W.J., Lin, H.L., Kan, H.D., et al., 2016. Ambient temperature and the risk of preterm birth in guangzhou, china (2001−2011). Environ. Health Perspect. 124 (7), 1100.
Hwang, B.F., Lee, Y.L., Jaakkola, J.J.K., 2011. Air pollution and stillbirth: a population-based case–control study in taiwan. Environ. Health Perspect. 119 (119), 1345–1349.
Kilinc, M.F., Cakmak, S., Demir, D.O., Doluoglu, O.G., Yildiz, Y., Horasanli, K., et al., 2016. Does maternal exposure during pregnancy to higher ambient temperature increase the risk of hypospadias? J. Pediatr. Urol. 12 (6), 407.e1.
Liang, Z., Yan, L., Ma, Y., Lei, Z., Xue, Z., Li, L., et al., 2016. The association between ambient temperature and preterm birth in Shenzhen, China: a distributed lag non-linear time series analysis. Environ. Health 15 (1), 84.
Listed, N., 1977. Who: recommended definitions, terminology and format for statistical tables related to the perinatal period and use of a new certificate for cause of perinatal deaths. Acta Obstet. Gynecol. Scand. 56 (3), 247.
Marlow, N., Wolke, D., Bracewell, M.A., Samara, M., 2005. Neurologic and developmental disability at six years of age after extremely preterm birth. N. Engl. J. Med. 352 (1), 9–19.
Nauels, A., 2014. Climate Change 2013: The Physical Science Basis. Contribution of Working Group I to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. Contribution of Working Group I to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change, Climate Change 2007: The Physical Science Basis.
Patrizia, S., Adele, L., Federica, A., Manuela, D.S., Marina, D., Paola, M., 2013. Effect of ambient temperature and air pollutants on the risk of preterm birth, rome 2001-2010. Environ. Int. 61 (4), 77–87.

Ramos, S.Z., Waring, M.E., Leung, K., Amir, N.S., Bannon, A.L., Moore Simas, T.A., 2017. Attempted and successful vacuum-assisted vaginal delivery by prepregnancy body mass index. Obstet. Gynecol. 129 (2), 311.

Roberts, S., 2004. Interactions between particulate air pollution and temperature in air pollution mortality time series studies. Environ. Res. 96 (3), 328.

Shulman, A., Hauser, R., Lipitz, S., Frenkel, Y., Dor, J., Bider, D., et al., 1998. Sperm motility is a major determinant of pregnancy outcome following intrauterine insemination. J. Assist. Reprod. Genet. 15 (6), 381–385.

Solomon, S., Qin, D., Manning, M., Chen, Z., Marquis, M., Averyt, K., et al., 2007. Summary for policymakers. Climate Change 2007: The Physical Science Basis. Contribution of Working Group I to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change. Contribution of Working Group I to the Fourth Assesment Report of the Intergovernmental Panel on Climate Change, Climate Change 2007: The Physical Science Basis.

Strand, L.B., Barnett, A.G., Tong, S., 2012. Maternal exposure to ambient temperature and the risks of preterm birth and stillbirth in brisbane, australia. Am. J. Epidemiol. 175 (2), 99–107.

Vicedo-Cabrera, A.M., Olsson, D., Forsberg, B., 2015. Exposure to seasonal temperatures during the last month of gestation and the risk of preterm birth in stockholm. Int. J. Environ. Res. Public Health 12 (4), 3962.

van Vliet, E.O., Askie, L.A., Mo, B.W., Oudijk, M.A., 2017. Antiplatelet agents and the prevention of spontaneous preterm birth: a systematic review and meta-analysis. Obstet. Gynecol. 129 (2).

Zou, B., Zhan, F.B., Zeng, Y., 2011. Maternal sulfur dioxide exposure and the risk of low birth-weight babies. Wei sheng yan jiu = J. Hyg. Res. 40 (5), 638.